UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/038,899	01/08/2002	Kokichi Kikuchi	216432US0XDIV	3573

22850 7590 08/05/2004

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/038,899	KIKUCHI ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-25* is/are pending in the application.

4a) Of the above claim(s) *14-18 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 05/17/04 has been acknowledged.

Claims 21-25 are newly filed claims.
Claims 19 21-25 are examined in this office action

This application contains claims 14-18, and 20 drawn to an invention nonelected with traverse in the reply filed on 09/02/03. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 19 and 21-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Nature of Invention:

The instant invention relates to a method for preventing or treating gastric cancer by administering into a patient cytotoxic T-lymphocytes (CTL), which has been activated with gastric cancer antigen protein (SEQ ID NO:1, SEQ ID NO:2).

Breadth of Claims and Guidance Provided in the Specification:

The scope of the invention as claimed encompasses preventing or treating a gastric cancer by administering CTL, which has been activated with gastric cancer antigen proteins (Seq ID NO:1 and 2) present in a human gastric cancer cell. At best the specification as filed teaches isolation of a polypeptide fragment comprising 10-12 amino acid sequences (SEQ ID NO: 1 and 2) which binds to HLA-A31 and is capable of inducing a cytotoxic T-cell that targets gastric cancer cells **in-vitro**. However, the specification as filed fails to disclose that administration of CTLs activated by SEQ ID NO:1 or SEQ NO:2 peptides would prevent or treat gastric cancer any gastric cancer patient.

State of Art and Predictability

The treatment of cancers is considered highly unpredictable because various genetic and etiological factors govern the development of a cancer. Antigens unique to individual tumors not only encompass mutated or rearranged oncogenes, tumor suppressor genes and viral genome encoded proteins but also the over expressed differentiation antigens or embryonic antigens (Shu et al, JAMA 278(22):1972-81, 1997 table 20.1, 20.2, page 1975-76). Down regulation of expression of antigens in cancer cells also represent a problem for the development of immuno-therapies because of the possible immunoselection of non-expressing tumor clones. For this reason an ideal target for the immune destruction is a protein that is essential for the malignant phenotype (Rosenberg, Immunity, 10:281-287, 1999). The state of the art clearly suggests that there is critical need to develop diversity of strategies and more efficient methods for identifying tumor specific antigens (Pardoll et al Curr. Opin. Imm. 10:588-594, 1998, page 592, col.2 para.3). Despite considerable advances in the understanding of the basic mechanisms underlying immune non responsiveness, the specific cellular immunological mechanisms that tumor cells exploit to avoid CTL mediated rejection is still not very well known (Antonia et al, Crit. Rev. Onc. 9(1):35-41, 1998 page 35, page 38, col.2, para.2). In addition the efficacy of tumor infiltrating lymphocytes is limited because tumor antigen that are targets for the effector cells are not well defined and infused cells have sub-optimal in-vivo survival and function, along with the poor localization of T cells to tumor sites (Yee et al, Curr. Opin. Imm. 9:702-

708, 1997). The art at the time of filing concluded that development of cancer immunotherapies based on the molecular characterization of tumor antigens is highly unpredictable and is in its early stages of development. The selection of target antigen or epitope for directing therapy will need to be considered in the light of a number of factors including: i) the prevalence of antigen expression by tumor cells, ii) the feasibility of isolating antigen specific T-cells from patients and iii) potential for the adoptive transferred antigen specific T-cells to induce toxicity in normal tissues (Rosenberg, Immunity 10:281-287, 1999, Yee et al, Curr. Opin. Imm. 9:702-708, 1997).

In addition F4.2 (a gastric cancer antigen) is the only art recognized antigenic peptide found in the human gastric cancer which induces HLA-A31-restricted autologous CTL response in TcHST-2 clonal T-cells (Nabeta et al Jpn. J. Cancer Res. 91;616-621, 2000, see page 620 col.2). The instant specification fails to identify all gastric cancer specific peptides that bind to all kinds of HLA molecule to induce a CTL response against the target gastric cancer cells in-vitro or in-vivo. Furthermore only 16.5% gastric cancer patients are positive for HLA-A31 expression (see Nabeta et al, page 617 col.2). Therefore to elicit a CTL response in the tumor cells lacking HLA-A31 expression one skill in the art would have to genetically modify the HLA-A31 negative tumor cells to express HLA-A31 genes (Suzuki et al J. Immunol. 163:2783-2791, 1999 see page 2783, col.2).

Response to arguments

The applicant argues that claim 19 has been amended to define the HLA molecule as HLA-A3I and the scope of the gastric cancer antigen has been limited to the amino acid sequence of SEQ ID NO:1 and SEQ ID NO:2. Regarding the in-vivo treatment of the gastric cancer the applicant argues that the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation. The applicant argues that even though the disclosure is only limited to in-vitro generated CTL response a skill artisan may practice the claimed invention from disclosure coupled with information known in the art regarding cell transfer therapy as practiced in cancer therapy. The applicant argues that the Nabeta et a1, Jpn. J. Cancer

Res., 91, 616-62 1 (2000), in which the present inventors have demonstrated that immunotherapy has a significant rate of recovery compared to mortality, therefore, immtmotherapy does possess efficacious advantages. The applicant concluded that invention as claimed is fully enabled by the specification and common knowledge available in the art.

However, applicant's arguments are found NOT persuasive because applicant's argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). In the instant case the specification as filed fails to provide any evidence that establishes that the administration CTL induced by gastric cancer antigens (SEQ ID NO:1 and 2) into a subject prevent or treat the gastric cancer in a patient. At best the specification as filed teaches isolation of a polypeptide fragment comprising 10-12 amino acid sequences (SEQ ID NO: 1 and 2) which binds to HLA-A31 and is capable of inducing a cytotoxic T-cells that targets gastric cancer cells **in-vitro**. In addition Nabeta et al (Jpn. J. Cancer Res., 91:616-62, 2000), does not teach the administration of gastric cancer antigen (SEQ ID NO:1 and 2) induced CTL to i) prevent gastric cancer in non-cancer patient or ii) to treat gastric cancer in a cancer patients. On the contrary Nabeta et al teaches that only 16.5% gastric cancer patients are positive for HLA-A31 expression. Therefore it is unclear how the instant invention (as filed) enables ones skill in the art to generate CTL immune response even in in-vitro to the claimed gastric antigen peptides (SEQ ID NO:1 and 2), wherein the cells don not express HLA-A31. Furthermore considering the unpredictability in the art of cancer treatment and limited amount of guidance provided in the instant specification, it is highly unpredictable that the invention as claimed could be exercised without further undue experimentation. The CTL based cancer prevention or treatment is not considered routine in the art and without sufficient guidance to a specific therapeutic gene the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the

accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to ***(571) 272-0547.***

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance.

Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306.**

Sumesh Kaushal
Examiner GAU 1636

JEFFREY FREDMAN
PRIMARY EXAMINER
7/3/07